Descriptive study of conversion ratios between conventional opioids and methadone in pediatric pain: the RUMPOH-1 study

Élise Druon[1,2], Tanya Santella[3], Catherine Corriveau[4], Kathryn DeKoven[3], Edith Villeneuve[3], Marie-Joëlle Doré-Bergeron[5] , Jean-François Delisle[1,6], Flaviu Mosora[1,6]

[1]Unité de Recherche en Pratique Pharmaceutique, Département de pharmacie, Centre Hospitalier Universitaire Sainte-Justine (CHUSJ), Montréal (QC), Canada
[2] Pharmacy student, Lille Pharmacy Faculty, Lille, France
[3]Pediatric anesthesiologist, Centre Hospitalier Universitaire Sainte-Justine (CHUSJ)
[4]Pediatric pain registered nurse, Centre Hospitalier Universitaire Sainte-Justine (CHUSJ)
[5]Pediatrician, Centre Hospitalier Universitaire Sainte-Justine (CHUSJ)
[6]Pharmacist, associate clinician, pharmacy department, Centre Hospitalier Universitaire Sainte-Justine (CHUSJ)

INTRODUCTION

- The pain management team at the Centre Hospitalier Universitaire Sainte-Justine (CHUSJ) has over a decade of experience using methadone for a wide variety of pediatric pain patients.
- Methadone has **distinct pharmacological properties** when compared to conventional opioids:
  - Appealing for nociceptive and neuropathic pain
  - Varied routes of administration available
  - Long half life and long action even as an oral liquid
- Single other study establishing a **universal conversion ratio** between converntional short-acting opioids (CSO) and methadone in pediatrics[1].
- Conversion ratios **increase** with CSO dose in adults[2].

OBJECTIVES

Primary objective: describe **conversion ratios between CSO and oral methadone**

Exploratory objective: describe the time **to methadone dose stabilisation** in relation to CSO doses

METHODS

- Retrospective descriptive review
- Patients aged 3mo to 18yo treated with IV methadone at our facility between January 1st 2011 and March 31st 2023
- Patients identified through our pharmacy records
- Methadone used for treatment of nociceptive, neuropathic or mixed type pain
- Exclusion criteria:
  - Patients on the neonatal ward
  - Patients treated with methadone for opioid use disorder
  - Patients in which methadone steady-state was not reached following conversion (5 days)
- Descriptive statistics

RESULTS

Table 1: Patient characteristics

	Patients (N=65) (%)
Age (years)	10.6
Males	39(60)
Underlying diagnosis	
Sarcoma	10 (15.4)
Acute myeloid leukemia	6 (9.2)
Other	49 (75)

	Patients (N=65) (%)
Weight (kg)	
0-20	13 (20)
20-40	22 (34)
>40	30 (46)
Opioid pre-methadone*	
Morphine	13 (18.1)
Hydromorphone	42 (58.3)
Fentanyl	16 (22.2)
Sulfentanyl	1 (1.4)

Table 2: Initial conversion ratios between CSO and oral methadone (under 40kg)

Conversion ratio	Overall population n=35 n (%)	Oral morphine equivalents		
		Low CSO doses (0-3mg/kg/day) (n=19) n (%)	Inter. CSO doses (3-10mg/kg/day) (n=10) n (%)	High CSO doses (>10mg/kg/day) (n=6) n (%)
0-3:1	5 (14.2)	**5 (26.3)**	0	0
3.01-5:1	5 (14.2)	**5 (26.3)**	0	0
5.01-10:1	5 (14.2)	**3 (15.8)**	**2 (20)**	0
10.01-15:1	7 (20)	**4 (21)**	**3 (30)**	0
15,01-20:1	3 (8.6)	1 (5.3)	**2 (20)**	0
>20:1	10 (28.6)	1 (5.3)	**3 (30)**	**6 (100)**

Table 3: Initial conversion ratios between CSO and oral methadone (40kg or more)

Conversion ratio	Overall population n=30 n (%)	Oral morphine equivalents (mg/day)			
		0-100 (n=11) n (%)	101-300 (n=8) n (%)	301-600 (n=7) n (%)	>601 (n=4) n (%)
0-3:1	3 (10)	**3 (27.3)**	0	0	0
3.01-5:1	3 (10)	**3 (27.3)**	0	0	0
5.01-10:1	4 (13.3)	**4 (36.4)**	0	0	0
10.01-15:1	3 (10)	**1 (9)**	**1 (12.5)**	**1 (14.3)**	0
15,01-20:1	3 (10)	0	**2 (25)**	**1 (14.3)**	0
>20:1	14 (46.7)	0	**5 (62.5)**	**5 (71.4)**	**4 (100)**

REFERENCES

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3. College of Physicians and Surgeons of British Columbia. Methadone for Analgesia Guidelines updated February 22nd 2019.

DISCUSSION

- 45 patients excluded for reasons of
  - Indication (6), lack of data (3),<48h treatment (8)
  - Other patients excluded because of age/study period
- Methadone often initiated in a pain escalation context
  - Ratios decrease between initiation and Day 5
- Wide variety of conversion ratios can be seen in both conversion groups (under/over 40kg)
  - Often driven by patient's pain and tolerance profile
- Efficient long term treatment for complex pain
  - Treatment duration mean 185 days (79 days median)
  - 40% of patients on methadone until death
- Universal conversion ratio described in pediatrics of 23.7:1 by Fife et al.
  - 65% of our patients have ratios <20:1
  - 38% of our patients have ratios <10:1
- Reaching steady-state is important especially for higher initial CSO doses
  - High conversion rate variability
- Strenghts:
  - Large sample size
  - Heterogenous population
  - Variety of treated conditions
  - Outpatient medication service assured by the CHUSJ, assuring medical record reliability
- Limitations
  - Retrospective nature of the study
  - Difficulty standardizing adverse events data collection in medical charts

CONCLUSION

- Methadone is a very useful tool in the arsenal of intractable pediatric pain and provides a durable analgesia
- Data scarcity does not allow for a statistical conclusion on standardized ratio in this population
- Conversion ratios increase in proportion to initial CSO doses in pediatric patients
- The 5 day conversion period is needed for patients with intermediate/high initial CSO doses

Contact : Flaviu Adrian Mosora flaviu.adrian.mosora.hsj@ssss.gouv.qc.ca ;

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